In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: September 24, 2014

M.R., a minor, by and through his natural parent and guardian, ANN ROBERTS, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	**PUBLISHED** No. 10-639V Special Master Dorsey Entitlement; Diphtheria-Tetanus-Acellular-Pertussis (DTaP) Vaccine; Hemophilus Influenzae Type b (Hib) Vaccine; Measles Mumps Rubella (MMR) Vaccine; Varicella Vaccine; Prevnar Vaccine; Seizure Disorder.

Lawrence Gene Michel, Kennedy, Berkley, et al., Salina, KS, for petitioner.
Alexis B. Babcock, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

I. Introduction

On September 23, 2010, Ann Roberts ("petitioner"), as the parent and natural guardian of M.R., a minor, filed a petition for compensation under the National Vaccine Injury Compensation Program ("the Program"[2]), alleging that the diphtheria tetanus acellular pertussis ("DTaP"), hemophilus influenzae-type b ("Hib"), measles mumps rubella ("MMR"), and varicella vaccinations M.R. received on February 21, 2008, and a Prevnar vaccination he

[1] Because this published ruling contains a reasoned explanation for the action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002, § 205, 44 U.S.C. § 3501 (2006). In accordance with the Vaccine Rules, each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b); 42 U.S.C. § 300aa-12(d)(4)(B)(2006). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted ruling. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be redacted.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (hereinafter "Vaccine Act" or "the Act"). Hereafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

received on March 17, 2008, caused M.R. to suffer from a seizure disorder. Petition ("Pet.") at 1-2. Respondent recommended against compensation, stating that petitioner has not presented preponderant evidence that the vaccinations caused M.R.'s injuries. See Respondent's Rule 4 Report ("Resp't's Report"), Dec. 20, 2010, at 12.

The parties submitted expert reports in support of their respective positions. Petitioner filed several reports from Dr. Dwight L. Lindholm. Petitioner's Exhibits ("Pet'r's Ex.") 2, 11, 19, 20, 23 and 28. Respondent filed expert reports from Dr. Max Wiznitzer and Dr. Mark S. Korson. Respondent's Exhibits ("Resp't's Ex.") A, C, N.

A hearing was held on December 4-5, 2013, during which the parties' experts testified. Petitioner filed a post-hearing brief on April 4, 2014, and respondent filed her post-hearing brief on May 19, 2014. Petitioner filed a reply to respondent's post-hearing brief on June 23, 2014. The matter is now ripe for adjudication.

After a review of the entire record, §300aa-13(a)(1), the undersigned finds petitioner has provided preponderant evidence that M.R.'s Prevnar vaccine caused his seizure disorder, which satisfies her burden of proof under Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1280 (Fed. Cir. 2005). See also Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1324 (Fed. Cir. 2006). Accordingly, petitioner is entitled to compensation.

II. Issues to be Decided and Factual Summary

A. Issues to Be Decided

Prior to the hearing, the parties filed a joint submission stating that no substantive factual issues exist and identifying the issues not in dispute. The parties agree that M.R. received a series of vaccinations on February 21, 2008, and March 17, 2008; that he was hospitalized on April 29, 2008, with a new onset of seizures; and that he has suffered from the residual effects of the seizures for greater than six months. See Joint Submission ("Jt. Sub.") at 3. The parties also agree that, to the extent that M.R. suffers from a mitochondrial disorder, the vaccinations did not cause such disorder. See Order, November 18, 2013.

The issue is whether there is preponderant evidence that M.R.'s February 21, 2008 and/or March 17, 2008 vaccinations caused his seizure disorder and related symptoms. See Jt. Sub. at 3; Transcript ("Tr.") at 5.

B. Summary of Facts[3]

M.R. was born healthy at full term on January 19, 2007. Pet'r's Ex. 3 at 79. He met the appropriate developmental milestones and his growth parameters were normal. Pet'r's Ex. 4 at

[3] This Summary of Facts section only contains a review of the most relevant facts, although the undersigned has considered the record as a whole in reaching her decision in this ruling. A more detailed recitation of the facts may be found in Respondent's Rule 4 report and in the parties' respective post-hearing briefs.

120-28.

On February 12, 2008, at 13 months old, M.R. was admitted to Memorial Hospital for respiratory syncytial virus (RSV) bronchiolitis.[4] Pet'r's Ex. 4 at 277. M.R. did not suffer from any RSV complications and was discharged on February 14, 2008. Id. M.R. was seen by Dr. Shelley Overholt on February 21, 2008, where he was determined to be a well-baby. Id. at 119. On that day, he received the DTaP, Hib, MMR, and Varicella vaccinations. Id.

After receiving the vaccinations on February 21, 2008, M.R. began having diarrhea. Pet'r's Ex. 4 at 119. On February 25, 2008, Dr. Overholt saw M.R. for continued complaints of diarrhea. Id. Petitioner was concerned that M.R. might have an IgA deficiency[5] because M.R.'s older brother had a prior history for that condition. Id. Accordingly, Dr. Overholt recommended IgA testing for M.R. Id.

On February 28, 2009, petitioner called to report that M.R. had not improved. Dr. Overholt prescribed probiotics and Pepto-Bismol. Pet'r's Ex. 4 at 277. On March 17, 2008, M.R. was again seen by Dr. Overholt, who described M.R. as normal, "happy, walking everywhere, and interacting." Id. at 117. M.R. received his Prevnar vaccination on the same day. Id.

During the first week of April 2008, M.R.'s parents noticed that he was experiencing ataxia[6] and was falling. Pet'r's Ex. 1 at 2. M.R.'s day care provider reported that he had fallen down stairs around the same period of time.[7] Tr. 35-36. Petitioner did not make a connection between M.R.'s clumsiness and the vaccinations because she thought that her son "was going through a clumsy stage." Id. at 22.

On April 28, 2008, M.R. suffered a tonic-clonic seizure while at home. Pet'r's Ex. 4 at 267. The next morning, his parents took him to Memorial Hospital. Id. at 267, 182. After experiencing additional seizures while at Memorial Hospital, M.R. was transferred to Wesley Medical Center ("WMC"). Pet'r's Ex. 4 at 267; Pet'r's Ex. 5 at 372. Upon admission to WMC, petitioner reported that M.R. had been falling. Pet'r's Ex. 4 at 267. Petitioner, who is a physical therapist, noted that M.R.'s balance was not as steady as compared to his brother at the same age.

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[4] Respondent's expert, Dr. Wiznitzer, testified that RSV did not play any causal role in M.R.'s development of ataxia or seizures. Tr. 268.

[5] IgA is a part of the immune system that protects one from viruses and illnesses. Tr. 47. IgA deficiency means that an individual is more prone to infections, including upper respiratory and gastrointestinal-type infections. Tr. 65.

[6] Ataxia is defined as "failure of muscular coordination; irregularity of muscular action." Dorland's Illustrated Medical Dictionary ("Dorland's"), 170 (32nd ed. (2012)).

[7] Other sources indicate various times for these events. See Tr. 36, 38 (Dr. Shoffner's history suggests that the balance and falling issues occurred 48 hours prior to onset of seizure).

Pet'r's Ex. 5 at 389, 402. She also noted that M.R. had been "clumsy" the "last couple of weeks." Id. at 389, 402. M.R. also had a history of nasal congestion and a slight bruise on his forehead. Id. at 402.

Upon admission to WMC, M.R. was seen by pediatric neurologist Dr. Dwight Lindholm. Tr. 64. Petitioner told Dr. Lindholm that, in hindsight, M.R. had been falling down more frequently and had been acting clumsier over the last two weeks.[8] Pet'r's Ex. 6 at 549. Consequently, Dr. Lindholm opined that M.R.'s neurological difficulties started about mid-April 2008. Tr. 68. Up until then, M.R. had had no delays in gross motor skills, fine motor skills, or speech. Id. Dr. Lindholm concluded that M.R. had experienced ataxia and seizures of recent onset, "following vaccinations." Pet'r's Ex. 4 at 269.

An electroencephalography ("EEG") of M.R.'s brain was performed on May 1, 2008, which Dr. Lindholm interpreted as abnormal. Tr. 73-74. The presence of higher voltage slow-waves of the bi-occipital regions indicated that M.R.'s brain was unable to slow down after seizure spikes to help prevent further seizures. Tr. 74. MRIs of the brain performed on May 1, 2008, and May 6, 2008, were interpreted as normal. Pet'r's Ex. 8 at 990, 993. The cerebral spinal fluid (CSF) analysis performed on May 1, 2008, was also normal. A repeat CSF analysis on May 7, 2008 was abnormal in that red blood cells were present. Pet'r's Ex. 8 at 976. By May 7, 2008, Dr. Lindholm had ruled out several possible etiologies for M.R.'s seizures, including infection and head trauma. Tr. 77. After ruling out other possible causes, Dr. Lindholm believed that M.R. had an autoimmune response to the vaccines which he believed caused M.R.'s seizures. Tr. 77, 88-89. On May 10, 2008, M.R. was discharged from the hospital on steroids and Keppra, among other medications. Pet'r's Ex. 6 at 548. Since then, Dr. Lindholm has continued to see M.R. as an outpatient every four months. Tr. 31.

Dr. John Shoffner, a mitochondrial specialist, saw M.R. on August 14, 2008. Pet'r's Ex. 9 at 1355-73. M.R. underwent genetic testing and lab work. Id. The results of the testing showed that M.R. had lactic acidemia and increased alanine, indicating a mitochondrial disorder. It was confirmed that M.R. had an IgA deficiency. Pet'r's Ex. 9 at 1368.

At the hearing, petitioner testified that M.R. is currently in school performing at grade level, although he has trouble keeping up with other students. Tr. 54. M.R. is prone to concussions and is unable to play football, wrestle, or engage in any activity that might result in injury to his head. Tr. 31, 33. M.R. still requires medication, including Keppra, levocarnitine, LiQsorbCoQ10, Diastat, and Ativan. Tr. 31, 41; Pet'r's Ex. 29 at 2. M.R. has not been hospitalized for seizures since 2011, although EEGs show that he continues to experience seizures. Tr. 41-42. Both petitioner and Dr. Lindholm believe that M.R.'s condition has improved since 2008. Tr. 43, 103-05; Pet'r's Ex. 29 at 2.

[8] This is inconsistent with the previous assertion that M.R.'s balance and falling issues occurred during the first week of April. However, petitioner subsequently explained that she did not have a calendar while she was at WMC and she gave the best information that she could at the time. See tr. 36.

III. Discussion

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons." Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344). "The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Id.

A. Standards for Adjudication

Petitioner's burden of proof is a preponderance of the evidence. § 300aa-13(a)(1). The preponderance of the evidence standard, in turn, has been interpreted to mean that a fact is more likely than not. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 300aa-13(a)(1)(B).

To receive compensation under the Program, petitioner must prove either: (1) that M.R. suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that he suffered an injury that was actually caused by the vaccine. See §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccines were "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

B. Causation - Elements of Petitioner's Claim

Because petitioner does not allege that M.R. suffered a Table injury, she must prove that the vaccinations M.R. received caused his injury. To do so, she must establish by preponderant evidence: (1) a medical theory causally connecting the vaccine and M.R.'s injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for M.R.'s injury ("Althen Prong Two"); and (3) a showing of proximate temporal relationship between the vaccine and M.R.'s injury ("Althen Prong Three"). Althen, 418 F.3d at 1278; § 300aa–13(a)(1) (requiring proof by a preponderance of the evidence).

Petitioner cannot establish entitlement to compensation based solely on her own assertions. A vaccine claim award must be supported either by medical records or by the opinion of a competent physician. § 300aa-13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation . . . of petitioner's illness." § 300aa-13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' offered experts

and rule in petitioner's favor when the evidence weighs in her favor. Moberly, 592 F.3d at 1325-26.

i. Althen Prong One: Petitioner's Medical Theory

Under Althen Prong One, petitioner must set forth a medical theory explaining how the vaccine received could have caused the sustained injury. Althen, 418 F.3d at 1278; Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). Thus, petitioner must make a showing that the received vaccine can cause the alleged injury. Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006).

Petitioner's theory of causation need not be medically or scientifically certain, Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994), but it must be informed by "sound and reliable medical or scientific explanation." Id. at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("[t]he special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories"); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) ("[a]n expert opinion is no better than the soundness of the reasons supporting it") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

1. Petitioner's Expert, Dr. Lindholm

Dr. Lindholm, M.R.'s treating physician, is also petitioner's expert. Dr. Lindholm attended the University of Kansas medical school and graduated in 1978. Tr. 58; Pet'r's Ex. 10 at 3. He completed his pediatric residency at the University of Kansas and a three-year pediatric neurology fellowship at the University of Texas, Dallas. Pet'r's Ex. 10 at 4. He then completed fellowships in neurophysiology at the University of Texas, Southwestern, and neuromuscular studies at the Texas Scottish Rite Hospital in Dallas. Tr. 58. He is board certified by the American Board of Psychiatry and Neurology with special qualifications in child neurology. Tr. 58-59; Pet'r's Ex. 10 at 4. He is also board certified by the American Board of Pediatrics. Tr. 59; Pet'r's Ex. 10 at 4. In his private practice, Dr. Lindholm cares for children experiencing a wide range of neurological problems, including seizures, migraine headaches, autism, attention deficit/hyperactivity disorder, developmental problems, and behavioral problems. Tr. 59. Dr. Lindholm is also the director of the Muscular Dystrophy Association Clinic. Id. In addition to M.R., Dr. Lindholm has treated other patients with neurological complications following vaccines. Tr. 107-08.

Dr. Lindholm is not board certified in immunology but has attended continuing medical education sessions on the subject. Tr. 108. He has experience with autoimmune inflammatory response disorders and has treated patients with Sydenham's chorea, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections ("PANDAS"), Guillain-Barré syndrome ("GBS"), transverse myelitis ("TM"), and acute cerebellar ataxia of childhood.

Tr. 143. He has testified in child abuse cases involving head injuries, subdural hematomas, Shaken Baby syndrome, Erb's palsy, seizures and strokes. Tr. 60.

Dr. Lindholm testified that M.R. was born with a mitochondrial disorder and that the vaccines did not cause that disorder. Tr. 84. Testing revealed that M.R. had a low IgA level, and there was concern that he may have had an IgA deficiency. Tr. 87. Dr. Lindholm opined that M.R. was predisposed to an autoimmune response from the vaccines because of his low IgA level and mitochondrial disorder. Tr. 125. Moreover, Dr. Lindholm opined that the vaccines administered to M.R. on February 21, followed 24 days later by the Prevnar vaccine, resulted in an intensive vaccine antigen load. Tr. 88, 121. M.R.'s predisposition, plus the intensive vaccine antigen load, caused M.R. to have an "enhanced immune response" because his "immune system [was] overwhelmed." Tr. 121.

Dr. Lindholm posits a medical theory based on an autoimmune response of cross-reactivity[9] post-vaccination where "antibodies formed to fight infection cross-react with [M.R.'s] own cells." Pet'r's Ex. 23 at 13. "The cross-reacting antibody… [that is] trying to attack the… infectious particle of the vaccine …fits the antigen within the …neurons or blood vessels." Tr. 125-26. Because M.R. received a number of vaccines, Dr. Lindholm is unable to identify which vaccine, or which component of the vaccine, triggered the cross-reactivity. Tr. 126.[10]

Dr. Lindholm further explained his theory as it relates to the development of seizures. He states that the abnormal cross-reactivity process causes inflammation, which damages neurons, and the neurons become "sick" and fail to function properly. Tr. 97. The neuron membranes break down and calcium rushes into the neurons, causing them to "fire erratically," resulting in seizures. Id. When a few neurons start firing erratically, other neurons also begin to fire when they should not, causing more seizures. Id. Thus, one seizure causes additional seizures. Id.

Dr. Lindholm cited two articles for the proposition that, generally, patients with IgA deficiencies may be predisposed to autoimmune conditions. In the Firinu[11] article, the authors state that "autoimmune complications in the context of primary immunodeficiency diseases represent a well-known phenomenon." Pet'r's Ex. 26 at 41. In the Takahashi[12] article, the authors concur that some patients with IgA deficiencies develop autoimmune conditions. Pet'r's

[9] Dr. Lindholm's theory of cross-reactivity is referred to by Respondent's expert, Dr. Wiznitzer, as molecular mimicry. Tr. 232.

[10] Dr. Lindholm explained this immune response in more detail as set forth in his PowerPoint, filed as Pet'r's Ex. 23 at 12-14, and at the hearing. See tr. 94-99.

[11] D. Firinu et al., "An Uncommon Association of Antiphospholipid Syndrome, Selective IgA Deficiency and Resistant-to-Treatment Relapsing Polychondritis: Efficacy of Infliximab", 26 J. of Biological Regulators & Homeostatic Agents 785 (2012).

[12] Noriyuki Takahashi et al., "Selective IgA Deficiency Mimicking Churg-Strauss Syndrome and Hypereosinophilic Syndrome: A Case Report", 75 Nagoya J. Med. Sci. 139 (2013).

Ex. 26 at 37. Respondent provided an article by Yel[13] that also supports the principle that patients with IgA deficiency have a "tendency to develop…autoimmune conditions." Resp't's Ex. F at 4. Examples of conditions associated with IgA deficiencies include "thyroid disease, arthropathy, celiac disease, anemia, and systemic lupus erythematosus." Id. at 5. These articles did not, however, specifically address the issue of whether an IgA deficiency predisposed one to having a seizure disorder.

Dr. Lindholm cites a number of articles in support of his opinion that inflammation played a role in M.R.'s seizure development. The results of the Marchi[14] experimental animal study support Dr. Lindholm's testimony that an "inflammatory mechanism and blood brain barrier damage" are contributing causes of seizures. See Pet'r's Ex. 24 at 2; Tr. 93-94. Dr. Lindholm also cited the Vezzani[15] article, in which the authors state that "[i]nflammatory reactions occur in the brain in various CNS diseases, including autoimmune … and epileptic disorders." Pet'r's Ex. 27 at 15. The authors further state that the "role of inflammation in the pathophysiology of human epilepsy is still hypothetical, although this possibility is supported by abundant evidence." Id. at 24. This abundant evidence includes the effects of steroids on seizures; markers of inflammation in serum, CSF, and brain cells; increased presence of pro-inflammatory molecules in neurons of brain tissue obtained from patients treated for drug resistant epilepsies; blood brain barrier dysfunction seen in animal models and suspected based on changes seen on SPECT studies; specialized studies on CSF showing blood brain barrier dysfunction; and increased blood brain barrier permeability induced by seizures or inflammation, or both, allowing immunogenic matter into the brain. Id. at 24-25. Dr. Lindholm also provided an article[16] where the authors concluded that "growing clinical and experimental evidence suggests that inflammatory processes in the CNS play an important role in the pathophysiology of epilepsy." Pet'r's Ex. 27 at 32.

2. Respondent's Expert, Dr. Wiznitzer

Dr. Max Wiznitzer received his medical doctorate degree from the Northwestern University in 1977. Tr. 208; Resp't's Ex. B at 1. He then trained in pediatrics at Cincinnati Children's Hospital and completed a one-year fellowship in developmental disorders at the Cincinnati Center for Developmental Disorders. Tr. 208; Resp't's Ex. B at 1. He subsequently completed a three-year child neurology fellowship at the University of Pennsylvania Hospital and its affiliates for the adult program, as well as Children's Hospital of Philadelphia for the pediatrics program. Tr. 208-09. Dr. Wiznitzer gained experience with epilepsy, mitochondrial encephalomyopathy, and similar types of mitochondrial DNA-based disorders while completing his neurology residency. Id. at 209. After that training, he was involved in a major

[13] Leman Yel, "Selective IgA Deficiency", 30 J. Clin. Immunology 13 (2010).
[14] Nicola Marchi et al., "Efficacy of Anti-Inflammatory Therapy in a Model of Acute Seizures and in a Population of Pediatric Drug Resistant Epileptics", 6(3) PLoS ONE 1 (2011).

[15] Annamaria Vezzani & Tiziana Granta, "Brain Inflammation in Epilepsy: Experimental and Clinical Evidence", Epilepsia 46(11) 1724 (2005).

[16] Stephanie Auvin et al., "Inflammation Induced by LPS Enhances Epileptogenesis in Immature Rat and May be Partially Reversed by IL1RA", 51(3) Epilepsia 34-38 (2010).

mitochondrial disorders center with a well-respected lab. Id. at 210. He is board certified by the American Board of Psychiatry and Neurology in neurology with a special qualification in child neurology, as well as neurodevelopmental disabilities. Id; Resp't's Ex. B at 5. He is currently a professor of pediatrics, neurology, and international health at Case Western Reserve University. Tr. 210; Resp't's Ex. B at 2.

Dr. Wiznitzer sees patients at least six to seven half-days a week. Tr. 211. As an electrophysiologist, he also interprets EEGs. Id. He treats and diagnoses patients with seizure disorders, and treats patients with mitochondrial dysfunction. Id. Furthermore, Dr. Wiznitzer is a member of the Brighton Collaboration, an international vaccine safety network. Id. at 212. In this role, he has developed case definitions for potential adverse events following vaccination. Id.

Dr. Wiznitzer opined that the vaccinations in this case played no role in causing or aggravating M.R.'s seizures. Tr. at 213. While he conceded that vaccines are known to cause fever, and fever "can provoke [an] underlying seizure tendency," Dr. Wiznitzer does not believe that the vaccinations in this case caused epilepsy or "alter[ed] the natural history of epilepsy." Id. at 217. He has "never seen seizures due to an autoimmune process present as they did in this case." Id. at 238-39.

Dr. Wiznitzer disagreed with Dr. Lindholm's opinion regarding an enhanced autoimmune response because, according to Dr. Wiznitzer, the human body is continuously exposed to antigens. Tr. at 227-28. As such, the immune system is "constantly on guard…always vigilant" and can "take care of what's going on." Id. at 228. Moreover, he argued that any antigenic material deposited from the Prevnar vaccine would have been "processed by the body and gone within two weeks." Id. at 230. According to Dr. Wiznitzer, by the time that M.R.'s initial symptoms of clumsiness and ataxia occurred "in the middle of April," the immune response to Prevnar would have "already calmed down." Id.

Dr. Wiznitzer also disagreed with Dr. Lindholm's theory that cross-reactivity – or molecular mimicry – can be initiated by a pneumococcal vaccine, opining that there is no proof of homology. Id. at 232-33. Dr. Wiznitzer argued that if there is no homology, one "can't develop an autoimmune disorder that would attack the nervous system." Id. at 233.

In his expert report, Dr. Wiznitzer initially opined that M.R.'s seizure disorder was caused by a mitochondrial encephalopathy that resulted from a Complex V defect. Resp't's Ex. A at 5. However, at the hearing, Dr. Wiznitzer changed his opinion. At the time of writing his expert report, Dr. Wiznitzer had received and reviewed medical records only up to 2008 and was not aware of the child's current good health. Tr. at 216. He testified at the hearing that this course of improvement was not typical for a mitochondrial disorder. Id. The typical clinical course of a mitochondrial disorder is a stagnation or gradual deterioration of function as the energy systems fail. Id. Since M.R. did not fit this clinical picture, Dr. Wiznitzer no longer maintains that M.R. has a Complex V defect.

3. Respondent's Expert, Dr. Korson

Dr. Mark Korson attended medical school in Toronto. Tr. 169; Resp't's Ex. D at 1. He completed his pediatric residency at the Hospital for Sick Children in Toronto and a genetics and metabolic fellowship at the Children's Hospital in Boston. Tr. 169-70; Resp't's Ex. D at 1. He is board certified in clinical biochemical genetics. Tr. 170; Resp't's Ex. D at 1. Dr. Korson specializes in patients with a broad range of metabolic disorders, largely energy metabolism or mitochondrial disease. Tr. 170. He is a member of the American Board of Medical Genetics and a member of the Society for Inherited Metabolic Disease. Id.

Dr. Korson is the chief of the metabolic service at Tufts Medical Center in Boston. Tr. 169. He is also an associate professor of pediatrics and he codirects the North American Metabolic Academy, which is a one-week intensive training course on metabolic and mitochondrial diseases sponsored by the Society for Inherited Metabolic Diseases. Id. at 171. Dr. Korson has been caring for children with mitochondrial disorders since 1986, and about 25 to 30 percent of his patients are children with mitochondrial disorders. Id. at 171-72. He currently sees around 20 patients per week. Id. at 171.

Dr. Korson was not questioned about and did not offer an opinion on Dr. Lindholm's medical theory of causation. Tr. 199. Dr. Korson was offered as an expert on the issue of whether or not M.R.'s vaccinations played a role in causing, or otherwise affecting, his underlying mitochondrial disease. Id. at 173-74. Dr. Korson does not believe that M.R. has a mitochondrial disease, but instead believes that M.R. has a "mitochondrial dysfunction." Id. at 181, 200. Dr. Korson explained the difference between mitochondrial disease and dysfunction as follows: in cases of mitochondrial disease, there is "a defect within the mitochondrion," whereas in cases involving mitochondrial dysfunction, something else impairs mitochondrial function, such as medication or malnourishment. Id. at 281. In cases of mitochondrial dysfunction, the mitochondria function improves when the offending issue is addressed. Id. at 181-82.

Dr. Korson testified, and the parties stipulated, that M.R.'s vaccinations did not cause or aggravate any underlying mitochondrial disorder. Tr. at 174, 198.[17] Dr. Korson disagreed with Dr. Lindholm that M.R.'s mitochondrial disorder predisposed him to autoimmune-mediated seizures. Id. at 198.

Dr. Korson testified that, generally, patients with "mitochondrial disease or dysfunction have normal immunity, but their body decompensates in the fight, so that …it takes them… longer to get better." Id. at 183. Dr. Korson explained that mitochondrial diseases cause "defects in energy metabolism," so that the cells in the body are unable to produce sufficient energy for the needs of the body. Id. at 174.

[17] During a pre-hearing status conference, counsel for petitioner confirmed that, to the extent that petitioner's pre-hearing submission asserts that Dr. Lindholm's testimony would prove that M.R.'s mitochondrial disorder was caused-in-fact by his vaccinations, the pre-hearing submission was in error. Order, November 18, 2013. The parties ultimately agreed that M.R.'s vaccinations did not cause his mitochondrial disorder. Id.

4. Evaluation of the Evidence

As a medical theory, molecular mimicry has been generally accepted in other cases, albeit not in this context. See, e.g., Althen v. Sec'y of Health & Human Servs., 58 Fed.Cl. 270, 278-79 (2005) (finding that petitioner provided molecular mimicry as a reliable theory and the government expert agreed with the theory generally), aff'd, 418 F.3d 1274 (Fed. Cir. 2005); Keenan v. Sec'y of Health & Human Servs., No. 99-561V, 2007 WL 1231592, at *11 (Fed. Cl. Apr. 5, 2007) (finding that petitioner had proffered a medical theory, molecular mimicry, which logically connected the vaccine administered to the condition complained of by petitioner); Scott v. Sec'y of Health & Human Servs., No. 03-2211V, 2006 WL 2559776, at *18 (Fed. Cl. Aug. 21, 2006) (concluding that the proffered molecular mimicry theory sufficiently established the first prong of the Althen test). Respondent's expert, Dr. Wiznitzer, cited an article that describes the medical theory relied upon by Dr. Lindholm. See Resp't's Ex. I at 14.

Dr. Lindholm's testimony, bolstered by the Vezzani article, explains the proffered medical theory by which M.R.'s vaccinations can cause brain inflammation and seizures. Although Dr. Lindholm conceded that he was unable to prove homology, the undersigned finds that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program." Knudsen, 35 F.3d at 549. Moreover, "a paucity of medical literature supporting a particular theory of causation cannot serve as a bar to recovery." Andreu, 569 F.3d at 1379 (citations omitted).

The undersigned concludes that petitioner has provided preponderant evidence that the vaccinations M.R. received can cause a seizure disorder via the mechanism of cross-reactivity posited by Dr. Lindholm. Accordingly, petitioner has satisfied Althen Prong One.

ii. Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioner must prove "a logical sequence of cause and effect showing that the vaccination was the reason for [M.R.'s] injury." Althen, 418 F.3d at 1278. Petitioner is required to show that the vaccine M.R. received actually caused the alleged injury. Pafford, 451 F.3d at 1355-56. Petitioner need not make a specific type of evidentiary showing. That is, petitioner is not required to offer "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. See id. at 1325-26.

1. Petitioner's Expert, Dr. Lindholm

Dr. Lindholm provided five reasons to support his opinion that M.R.'s seizures were caused by an autoimmune response to his vaccines. Tr. 77-78. First, Dr. Lindholm believed that M.R. was predisposed to an autoimmune response due to his low IgA and his mitochondrial disorder. Id. at 88-89. Dr. Lindholm provided an article by Takahashi to demonstrate that patients with immunoglobulin deficiencies may have autoimmune diseases. See Pet'r's Ex. 26 at

33. The Firinu article further supports Dr. Lindholm's idea that low IgA predisposes one to autoimmune problems, as autoimmune diseases are more frequent in IgA deficient patients. Id. at 43.

Dr. Lindholm's second reason is based upon timing. M.R. developed ataxia, a neurological symptom, within 28 days of receiving his Prevnar vaccine.[18] Pet'r's Ex. 23 at 6. Dr. Lindholm argues that at the time M.R. received the Prevnar vaccination—24 days after his DTaP, Hib, MMR, and Varicella vaccinations—M.R. "would still have been in an intensified immune state." Id.; Tr. 88. Dr. Lindholm opined that two weeks to four weeks is "in the usual time range of a complication following vaccination." Pet'r's Ex. 20 at 3.

Third, M.R. did not respond to anti-seizure medications, but instead, had a dramatic response to the anti-inflammatory medication Prednisone, a steroid. Pet'r's Ex. 23 at 6; Tr. 89. Steroids such as Prednisone combat "abnormal antibodies … causing damage to neurons or blood vessels in the brain" after an autoimmune response. Tr. 145. Thus, Dr. Lindholm believes that seizure response to steroids is a good indication that an autoimmune process is the underlying cause of the seizures. Id. at 114.

After M.R. began taking Prednisone, a video EEG performed on May 7-9, 2008, showed improvement. Tr. at 110. While some medical records indicate that M.R. did not start taking Prednisone until May 8, 2008, Dr. Lindholm clarified that M.R.'s EEG procedure ran from May 7, 2008, until May 9, 2008. Pet'r's Ex. 8 at 1027; Pet'r's Ex. 28 at 5-6. M.R. began receiving Prednisone the morning of May 8, 2008, and his last seizure was recorded on the same date.[19]

Dr. Lindholm cited the Marchi article[20] in support of his argument that M.R.'s response to steroids indicates that M.R.'s seizures had an autoimmune etiology. Pet'r's Ex. 24. In that article, the authors evaluated the efficacy of glucocorticoids[21] in reducing the onset and the severity of status epilepticus in rats and concluded that glucocorticoids can effectively treat drug resistant seizures in children. See id. Dr. Lindholm's opinion is also supported by the Vezzani article, where the authors suggest that inflammation plays a role in epilepsy, based upon the

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[18] Dr. Lindholm used April 14th as the date of onset for M.R.'s ataxia. It would appear, however, that based on M.R.'s mother's testimony, the onset of the ataxia was, at the earliest, 15 days after receipt of the Prevnar vaccination, in early April 2008. Tr. at 35-56.

[19] Though a few of the doses were not specifically documented as administered to the patient, Dr. Lindholm explained that the nurse would only document if a dose was not administered. Tr. 114. As there were no such indications, M.R. probably received all of the doses of Prednisone ordered during the EEG. Id.

[20] Marchi at 1371. *See* n. 13.

[21] Glucocorticoids are a type of steroid hormone that acts as an anti-inflammatory drug. See Pet'r's Ex. 24 at 2; E. Tan, "Glucocorticoids", Huntington's Outreach Program for Education, at Stanford (June 15, 2002), http://web.stanford.edu/group/hopes/cgi-bin/wordpress/2010/06/glucocorticoids.

effect of anti-inflammatory drugs. See Pet'r's Ex. 27 at 24. Dr. Lindholm has also seen patients with autoimmune diseases respond to immune modulators such as steroids, as occurred in M.R.'s case. Pet'r's Ex. 23 at 9. Steroids reduce seizures by stabilizing the damage caused by autoimmune illnesses to the blood brain barrier. Tr. 93. Dr. Lindholm relied on the Marchi article to support his opinion that steroids effectively treat seizures caused by autoimmune responses. Tr. 93-94; Pet'r's Ex. 24 at 1-2. In M.R.'s case, "once the autoimmune process was shut down [with steroids], the Keppra alone was able to maintain seizure control." Pet'r's Ex. 28 at 8.

Fourth, Dr. Lindholm believed that M.R.'s CSF IgG index of 0.60 on May 7, 2008, evidenced inflammation of the central nervous system (CNS) and disruption of the blood brain barrier. Tr. 115. Dr. Lindholm has seen patients with an IgG index greater than 0.50 who have autoimmune diseases of the CNS. Pet'r's Ex. 23 at 9; Tr. 92-93. Dr. Lindholm agreed that 0.60 was accepted as a normal value but, in light of his clinical experience, Dr. Lindholm suspected an autoimmune etiology when an IgG is greater than 0.50. Tr. 92. According to an article written by Rudick,[22] IgG levels do not have to be greater than 0.85 to signify an autoimmune response. Pet'r's Ex. 21 at 15.

Dr. Lindholm acknowledged that M.R.'s albumin index was three, which is a normal value and which suggested that M.R.'s blood brain barrier was intact. Tr. 119. However, Dr. Lindholm argued that M.R. could have a "mostly intact blood brain barrier" and still "have a problem with increased IgG synthesis" in the CNS, indicating an inflammation or autoimmune disorder of the CNS. Id. at 119-20.

Lastly, Dr. Lindholm testified that he had ruled out other possible causes for M.R.'s seizure disorder. Tr. at 77. Testing for lupus was negative. Id. at 114. M.R. did not have vasculitis or ataxia telangiectasia. Id. at 115. M.R.'s differential diagnosis also included post-infectious encephalitis, similar to what is seen after mycoplasma pneumonia. Id. at 144. That condition, however, usually causes complex partial and generalized tonic-clonic seizures, not myoclonic seizures. Id. at 144-45. Dr. Lindholm also opined that viral etiologies were unlikely, as viral cultures on the spinal fluid were negative. Id. at 155. Likewise, Polymerase Chain Reaction ("PCR"), a very sensitive test for herpes simplex virus and cytomegaly virus, was performed on the spinal fluid and was negative. Id. at 154. Throat cultures for antistreptolysin O titer tests were also normal, indicating that M.R. did not have a post-strep infection. Id. at 155. M.R.'s CSF white blood cell count was normal, and if his seizures had been caused by a viral infection, one would expect to see an elevated white blood cell count. Id. at 153, 156. Another differential diagnosis was white matter disease, but this diagnosis was unlikely because M.R.'s brain MRI was normal. Id. at 158. Furthermore, there was no history of trauma or any abnormalities on the MRI to explain M.R.'s seizure disorder. Id. at 77.

[22] The authors characterized a high IgG index as levels greater than or equal to 0.67 in patients with multiple sclerosis. See Richard A. Rudick, et al., "Cerebrospinal Fluid Abnormalities in a Phase III Trial of Avonex (IFNβ-1a) for Relapsing Multiple Sclerosis," 93 Journal of Neuroimmunology 10 (1999).

Although Dr. Lindholm believes that M.R. has a mitochondrial disorder, and some patients with mitochondrial disorders have seizures, Dr. Lindholm does not believe that the mitochondrial disorder caused M.R.'s seizures. Pet'r's Ex. 23 at 17-18. Indeed, all of the experts agree that M.R.'s seizure disorder was not caused by his mitochondrial disorder. Tr. 174, 198. Dr. Lindholm did opine that M.R.'s mitochondrial myopathy made him more susceptible to an autoimmune reaction to the vaccinations, and also made M.R's seizures more difficult to treat. Id. at 130. This aspect of petitioner's case was not proven by a preponderance of the evidence, and thus does not form part of the basis of the undersigned's decision.

Dr. Lindholm acknowledged that he did not send M.R.'s CSF for auto-antibody testing to support or rule out vaccination causation because M.R. had already undergone two spinal taps, and Dr. Lindholm did not want to "unnecessarily subject" M.R. to such testing. Tr. at 120-21. In addition, Dr. Lindholm testified that because M.R. had been taking Prednisone for so long, the test results might not be reliable. Id.

2. Respondent's Expert, Dr. Wiznitzer

Dr. Wiznitzer provided rebuttal testimony in response to Dr. Lindholm's opinion. Dr. Wiznitzer opined that M.R. did not have an IgA deficiency at the time of his seizure onset, as he was too young to be diagnosed with this disorder, nor did M.R. have any "clinical features of an immunodeficiency" of an IgA deficiency. Id. at 225-26. He opined that M.R. had not had excessive illnesses which are usually seen in children with this disorder. Id. at 227. If M.R. had been older, his lab values would have been low, but he would not present a case of "classic IgA deficiency" because there was still a measurable level of IgA. Id. at 226.

Dr. Wiznitzer opined that the onset of M.R.'s neurological disorder did not occur until April 28, 2008, the date of M.R.'s first seizure. Tr. 217. Dr. Wiznitzer stated that M.R.'s clumsiness and falling two weeks prior to the seizure suggested unsteadiness instead of ataxia. Id. at 219. While Dr. Wiznitzer agreed that M.R. had myoclonic seizures, he also believed that M.R. had generalized tonic-clonic and atonic seizures. Id. at 223. While this is not a common presentation, Dr. Wiznitzer testified that he had seen the presentation before, although not in the "context of an autoimmune disorder." Id. Dr. Wiznitzer further testified that these types of seizures are not typically caused by vaccines. Id. at 225.

Dr. Wiznitzer disagreed that M.R.'s response to steroids explains the etiology of M.R.'s seizure disorder. Tr. 219. In Dr. Wiznitzer's opinion, the effective use of steroid medication in treating epilepsy is not attributable to its anti-inflammatory effect. Id. Rather, he opined that steroids stop seizures by changing the levels of certain hormones in the brain, modulating neurotransmitters or chemicals in the brain, and suppressing a nerve function. Id. at 220. He disagreed with Dr. Lindholm and stated that M.R. was not taking steroids when he underwent the video EEG on May 7, 2008. Id. at 244; Pet'r's Ex. 9 at 999. He believed that Prednisone was not administered to M.R. until one day after the video EEG was started, on May 8, 2008. Tr. 244. Accordingly, Dr. Wiznitzer opined that Dr. Lindholm's hypothesis – that is, that the improvement seen on the video EEG initiated on May 7, 2008, was due to the effect of steroids –

was not supported by the evidence.[23] Id.

Dr. Wiznitzer also disagreed with Dr. Lindholm's argument that M.R.'s IgG index of 0.60 indicated inflammation of the CNS. Tr. 233. Although Dr. Wiznitzer acknowledged that an elevated IgG index indicates that the body is producing immunoglobulin, he testified that M.R.'s IgG index of 0.60 was normal. Id. Nevertheless, Dr. Wiznitzer conceded that he had seen an index of 0.60 in children with autoimmune conditions, and that he had seen an IgG of 0.60 in the autoimmune condition of acute disseminated encephalomyelitis. Id. at 253.

Dr. Wiznitzer further disputed the argument that M.R. had an autoimmune disorder of the CNS. Tr. 236-38. M.R. had a normal albumin index, which to Dr. Wiznitzer, indicated that his "blood brain barrier [was] intact." Id. at 237-38. While Dr. Wiznitzer conceded that M.R.'s CSF analysis performed May 7, 2008, showed abnormally high red blood cells ("RBCs") of 80, he did not attribute the abnormally high result to inflammation. Id. at 250-51. Instead, he believed that the presence of RBCs was due to a "traumatic" spinal tap, where the needle caused trauma during the procedure.[24] Id. at 251. Assuming that there were RBCs present that were not due to trauma, Dr. Wiznitzer was equivocal as to the reason for their presence. He first testified that RBCs in M.R.'s CSF signified an autoimmune disorder of his CNS, but he later testified that it did not. Tr. at 237-38, 252.

Dr. Wiznitzer maintained that the Marchi article did not support petitioner's theory. Tr. at 240-41. That study examined an animal given a toxic agent, which led to the animal to develop seizures and an abnormal MRI. Id. at 241-42. By contrast, Dr. Wiznitzer did not believe that M.R. was given a toxin, or that M.R.'s blood brain barrier was disrupted. Id. at 242. Furthermore, Dr. Wiznitzer pointed out that M.R.'s brain MRI was normal. Id.

Finally, Dr. Wiznitzer did not believe that any clinical or lab evidence supported Dr. Lindholm's autoimmune response theory. Id. at 230. Dr. Wiznitzer testified that M.R. had a normal response, not an enhanced response as Dr. Lindholm opined, to the Prevnar vaccine. Id. at 231. Dr. Wiznitzer testified that M.R.'s pneumococcal vaccine antibody lab results, which showed a response to serotype 19, but not to serotypes 14 or 23, did not support the theory that M.R. exhibited a "super response or enhanced response" to the Prevnar vaccine. Id. Dr. Wiznitzer testified that this is the response that is expected. Id.

3. Respondent's Expert, Dr. Korson

Dr. Korson was initially retained when the parties disagreed as to whether M.R.'s vaccinations played a causal role in his mitochondrial disorder, and his opinion was offered to

[23] Dr. Lindholm rebutted Dr. Wiznitzer's testimony in a written response explaining that the steroids were administered to M.R. during the EEG. Dr. Lindholm stated that, according to the medical records, orders for the steroids and instructions for administration of those steroids were made during the time the EEG was conducted. See Pet'r's Ex. 28 at 5-6.

[24] The progress notes in the record from the spinal tap on May 7, 2008 do not reflect that any trauma occurred during the procedure. Pet'r's Ex. 8 at 854-60.

explain the relationship, if any, between M.R.'s vaccines and his mitochondrial disease. See Order, March, 2012, at 1; tr. 174; tr. 199. Ultimately, both parties agreed that vaccinations played no role in the development of M.R.'s mitochondrial disorder, and Dr. Korson did not opine on the existence of a causal connection between the vaccinations and M.R.'s seizures. Id.

4. Evaluation of the Evidence

As an initial matter, the undersigned finds that treating physicians are generally in the best position to determine the cause of a petitioner's condition, Capizzano, 440 F.3d at 1326, and that Dr. Lindholm's opinions are therefore particularly probative when viewed in that context. Even so, Dr. Lindholm's opinions would be unavailing under Althen Prong Two had he merely noted a temporal relationship between M.R.'s vaccinations and the onset of his ataxia and seizure disorder. See Moberly, 592 F.3d at 1323 (holding opinions of petitioner's treating physicians noting a temporal proximity insufficient under Althen Prong Two because none "drew a causal link" between vaccine and alleged injury). But, as enumerated above, Dr. Lindholm set forth specific factual reasons, based upon his experience and M.R.'s clinical course, to support his causal opinions. He also cited medical literature that bolstered his opinions, including the Marchi article, which documents a link between a response to steroids and an autoimmune etiology of seizures. Dr. Lindholm's contention that M.R.'s IgG evidenced an inflammation of the CNS was further bolstered both by Dr. Wiznitzer's statement that he has seen an index of 0.60 in children with autoimmune conditions, and also by the Rudick article, according to which the IgG index does not have to be greater than 0.85 to be considered abnormal.

Petitioner provided sufficient circumstantial evidence and reliable medical opinions to demonstrate, by a preponderance of the evidence, a logical sequence of cause and effect showing that the vaccinations were the cause of M.R.'s injury. Therefore, the undersigned finds that the petitioner has satisfied her burden under Althen Prong Two.

iii. Althen Prong Three: Medically Acceptable Timeframe

Under Althen Prong Three, petitioner must establish that M.R.'s injury occurred within a timeframe that is medically acceptable for the alleged mechanism of harm. Althen, 418 F.3d at 1278. Petitioner satisfies this prong by producing "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan v. Sec'y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008); see also Pafford, 451 F.3d at 1358 ("Evidence demonstrating petitioner's injury occurred within a medically acceptable time frame bolsters a link between the injury alleged and the vaccination at issue under the 'but-for' prong of the causation analysis.").

1. Petitioner's Expert, Dr. Lindholm

The onset of M.R.'s ataxia began within two to four weeks following his receipt of the Prevnar vaccination, which is "the usual time range of a complication following vaccination." Pet'r's Ex. 20 at 3. Dr. Lindholm testified that the onset of M.R.'s neurological symptoms

coincided with his ataxia, as noted by M.R.'s mother.[25] Tr. 67-68. According to Dr. Lindholm, the ataxia began on approximately April 14, 2008, 28 days following M.R.'s receipt of the Prevnar vaccination and 54 days after the vaccinations administered to M.R. on March 17, 2008. Id. at 79. Dr. Lindholm explained that the ataxia was a sign of the abnormal autoimmune response and a precursor of the seizures. Tr. 163.

According to the Vezzani article cited by Dr. Lindholm, the "patterns of induction of inflammatory molecules and their time course of activation… in brain tissue… depend[s] on the nature of the CNS injury." Pet'r's Ex. 27 at 16. More specifically, "the final outcome of inflammation on cell function is highly dependent on the extent to which cytokines are produced… [and] the length of time the tissue is exposed to inflammation[.]" Id. at 19.

2. Respondent's Expert, Dr. Wiznitzer

Dr. Wiznitzer did not find plausible the theory that M.R. experienced an autoimmune process that caused either ataxia or seizures within five to six weeks post-vaccinations, but agreed that he has seen ataxia caused by vaccinations within two weeks of a varicella vaccine. Tr. 261-64. He also testified that he has seen autoimmune conditions within four to six weeks after vaccination. Id. at 263. While Dr. Wiznitzer is aware of seizures with ataxia occurring four to six weeks after vaccines in case reports related to patients with another inflammatory condition, acute disseminated encephalomyelitis, he testified that the clinical course in those cases is different than M.R.'s case. Id. at 263-64.

3. Evaluation of the Evidence

The undersigned finds M.R.'s mother's (petitioner) and Dr. Lindholm's testimony persuasive, and therefore finds that the onset of M.R.'s neurological symptoms began between the first week of April 2008, when M.R. began falling down and acting clumsier, and April 14, 2008, the date of onset according to Dr. Lindholm. Tr. 22, 79. Thus, onset was between 15-22 days after M.R. was administered the Prevnar vaccine. Petitioner asserts that this timeframe is medically acceptable according to Dr. Lindholm's theory of autoimmune response and cross-reactivity. Petitioner's Post-Hearing Brief ("Post-Hearing Br.") at 8. Respondent's expert, Dr. Wiznitzer, also agrees that a two to four week onset is a medically acceptable time frame after vaccination. Tr. 261-64. Onset was over 40 days after receipt of the other vaccinations, beyond the two to four week time-frame referenced by Dr. Lindholm.

As the Vezzani article posits, inflammatory molecules and their time course of activation depend on various factors, including the nature of the CNS injury. Pet'r's Ex. 27 at 16. Within two weeks of the Prevnar vaccine, M.R. began showing signs of ataxia. According to both Dr. Lindholm and Dr. Wiznitzer, ataxia can be a symptom of the autoimmune response that can lead to seizures. This timeline is consistent with autoimmune responses, as these reactions take longer to manifest. See Crosby v. Sec'y of Health & Human Servs., No. 08-799V, 2012 WL 3758430, at *4 (Fed. Cl. June 20, 2012) (accepting respondent's expert's citation of the IOM that

[25] At the hearing, petitioner testified that M.R.'s clumsiness began the first week of April. Id. at 22.

latency between a vaccination and the first symptom of illness should fall between 5 and 42 days to be considered credible).

In reaching his conclusion regarding causation, Dr. Lindholm relied on the temporal relationship established by the medical records between M.R.'s vaccinations and his autoimmune response. As such, he found that the timing of the onset of petitioner's ataxia was medically acceptable to infer causation. See Contreras v. Sec'y of Health & Human Servs., 107 Fed. Cl. 280, 299 (2012) ("[I]t is difficult to conceive of a treating physician who would conclude that a vaccine caused the petitioner's illness without also concluding that the onset of the illness was within a medically-acceptable time-frame.").

While a proximate temporal connection between a vaccination and an injury is insufficient, standing alone, to establish causation, Grant 956 F.2d at 1148, here, M.R.'s treating physician testified that the temporal connection between the Prevnar vaccine and M.R.'s injury is medically acceptable and concluded that petitioner had fulfilled the other two Althen prongs. See Capizzano, 440 F.3d at 1326 (finding evidence used to support one Prong can overlap to satisfy another Prong). Dr. Lindholm testified that M.R.'s onset of symptoms was medically acceptable based on his theory of autoimmune response and cross-reactivity. The undersigned concludes that petitioner has shown, by a preponderance of the evidence, that the injury occurred within a medically acceptable timeframe following the Prevnar vaccination, and that petitioner has therefore satisfied Althen Prong Three.

C. Alternative Causation

Because petitioner has established a prima facie case, she is entitled to compensation unless respondent can put forth preponderant evidence "that [M.R.'s] injury was in fact caused by factors unrelated to the vaccine." 42 U.S.C. § 300aa–13(a)(1)(B); see also Walther v. Sec'y of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007).

During the hearing, Dr. Wiznitzer opined, for the first time in the pendency of this case, that M.R.'s clinical course might be consistent with Doose Syndrome, a seizure disorder characterized by generalized tonic-clonic seizures, atonic seizures, and myoclonic seizures. Tr. 246, 249. Dr. Wiznitzer testified that he had had another patient with Doose Syndrome who had responded well to steroids, and that the syndrome is thought to be genetic in origin. Id. at 246-47. Dr. Wiznitzer added, however, that if M.R.'s prior seizures were complex partial seizures, as described by Dr. Lindholm, then Doose syndrome would be an unlikely diagnosis.[26] Id. at 247.

Assuming that Dr. Lindholm's description of M.R.'s seizures was accurate, Dr. Wiznitzer did not propose a diagnosis for M.R., other than to say that "there is something not right with the brain wiring." Id. at 250.

[26] Dr. Wiznitzer disagreed with Dr. Lindholm that M.R. had complex partial seizures, as diagnosed by Dr. Lindholm, based on "body movements and . . . isolated discharges on the video EEG." Id. at 249. Dr. Wiznitzer opined that there should have been a "clinical description of a complex partial seizure" in the medical records, but that such a description was absent. Id.

A thorough review of the medical records shows no mention of Doose Syndrome, and none of M.R.'s treating physicians referred to this diagnosis as a potential cause of M.R.'s seizure disorder. More importantly, Dr. Wiznitzer concedes that if Dr. Lindholm, the treating neurologist, was correct in his description of M.R.'s seizures, then Doose Syndrome is not an alternative explanation for M.R.'s seizure disorder.

The undersigned agrees with petitioner's position that Dr. Lindholm was in the best position to evaluate M.R.'s seizures, and his evaluation is entitled to deference. See Petitioner's Reply Brief to Respondent's Post-Hearing Brief at 4; Capizzano, 440 F.3d at 1326 (holding that treating physicians are likely in the best position to determine whether the vaccination was the reason for the injury). Accordingly, the undersigned finds that respondent has failed to provide preponderant evidence of an alternative cause of M.R.'s seizure disorder.

IV. Conclusion

Petitioner has provided preponderant evidence that the Prevnar vaccination M.R. received on March 17, 2008, caused him to suffer a seizure disorder. For the reasons discussed above, the undersigned finds that petitioner is entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/ Nora Beth Dorsey
Nora Beth Dorsey
Special Master